



Dkt. 0575/61020-A/JPW/PJP/PL

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Michael R. Rosen, et al

U.S. Serial No.: 09/505,458

Examiner: F. Oropeza

Filed: February 11, 2000

Group Art Unit: 3762

For: CARDIAC REMODELING

1185 Ave of the Americas
New York, New York 10036

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

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TECHNOLOGY CENTER H3700

Sir:

DECLARATION OF MICHAEL R. ROSEN, M.D., PURSUANT TO 37 C.F.R.
§1.132

I, Michael R. Rosen, hereby declare as follows:

1. I am an inventor of the subject matter claimed in the above-identified patent application.
2. I am a Professor of Pharmacology and Pediatrics at Columbia University, the assignee of record of the subject invention. I hold a Medical Doctor degree. A copy of my curriculum vitae is attached hereto as **Exhibit A**.
3. I have reviewed the Office Action issued by the United States Patent and Trademark Office on September 17, 2003 wherein the pending claims 1, 9-11, 20, 28-30,

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Exhibit 1

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39, and 47-49 are rejected under 35 U.S.C. 102(e) as being allegedly anticipated by Ben-Haim et al., U.S. Patent No. 6,363,279. I have additionally reviewed the subject application.

4. I understand that pending claims 1, 9-11, 20, 28-30, 39, and 47-49 are being rejected because the Examiner alleged that Ben Haim teaches a method of modifying the force of contraction of a heart by applying a non-excitatory electrical field to modify/alter/remodel the action potentials, the ionic pumps, and the channels of the heart. In addition, the Examiner stated that Ben-Haim's invention inherently controls the gap junction channels of the heart and that Ben Haim's invention teaches that refractory periods are modified by electrical stimulation.
5. I have reviewed the Ben Haim reference and also personally familiar with the work of Ben Haim. Ben Haim proposes that his device applies an electrical field to the heart, but this electrical field would not cause the heart to be excited and activated. Rather, the device discussed in Ben Haim is simply used to modify the plateau currents, resulting in what Ben Haim says is an increase in force of contraction. In contrast, the presently claimed invention in the

subject application applies an electrical stimulus to the heart that does excite it, resulting in altered activation, which must occur for the downstream channels to occur in gap junctions and ion channels. Because the device of Ben Haim's invention would not cause the heart to be excited, resulting in altered activation, the device would not necessarily induce ion channel remodeling or remodel gap junctions. The disclosure in Ben Haim is insufficient in showing how Ben Haim's device would actually induce ion channel remodeling and/or remodel gap junctions. Thus, the Ben Haim device would not necessarily induce ion channel remodeling or remodel gap junctions. Based on Ben Haim and the Winslow et al. reference, the latter of which merely describes conductance models which can incorporate gap junctions, Ben Haim would not inherently remodel gap junctions or induce ion channel remodeling for the reasons mentioned above.

6. The Ben Haim reference states that the configuration of his electrodes may be, as shown in Figure 2, two electrodes 34, 36, placed on opposite side, i.e. interior and exterior of the right atrium (See col. 28, lines 46-54). Ben Haim also states that electrode 34 may float inside the heart. (col. 28, lines 56-58). In another embodiment shown in Figure 2 two electrodes 37 may be applied along the heart wall. (See col. 28, lines 64-66). In another embodiment one

pair of electrodes are placed on the epicardium and a second pair placed inside the myocardium. (col. 29, lines 13-18). In another embodiment, shown in Figure 4B, a single column of electrodes 59 are placed along a heart segment 55. (col. 37, lines 7-10). Ben Haim states that the electrodes may be activated in pairs (col. 37, lines 15-17). None of these electrode configurations would, using the signals discussed by Ben Haim, necessarily result in inducing ion channel remodeling or remodeling of gap junctions.

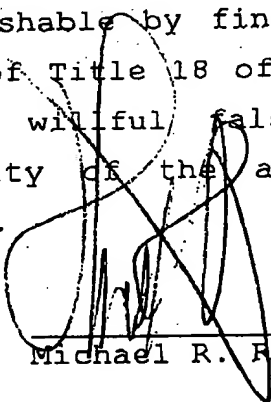
7. Also, the Ben Haim device would not necessarily alter the refractory period. While the Examiner asserts that Ben Haim discloses that refractory periods are altered by electrical stimulation, to the contrary, the electrical stimulation proposed by Ben Haim would not necessarily alter the effective refractive period. Ben Haim does not disclose that the electrical stimulation described therein would alter the effective refractory period, and such electrical stimulation would not inherently alter the effective refractory period. The presently claimed invention in the subject application claims a method to alter the effective refractory period (ERP). The ERP's in the myocardium are primarily determined by the recovery of excitability of sodium channels carrying the fast inward sodium current. This process is both voltage-

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and time-dependent. While the ERP may change consonantly with action potential duration and QT interval, ERP would not necessarily be altered. Thus, the electrical stimulation as described in Ben Haim would not automatically and necessarily alter the ERP.

8. I hereby declare that all statements made herein on my own knowledge are true and that all statements made herein on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

12-16-03
Date



Michael R. Rosen, M.D.